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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/644,080	UNGER ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 20 August 2003 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This is the First Office Action on the Merits of the application filed 20 August 2003 as a divisional of application 09/742,938 filed 21 December 2000, which is a divisional of application 08/841,169 filed 29 April 1997, which is a continuation-in-part of application 08/785,661 filed 17 January 1997, which is a continuation-in-part of application 08/640,554 filed 1 May 1996. The preliminary amendment canceling claims 2-104, which was filed concurrently with the application, is acknowledged. Claim 1 is pending and under consideration.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,638,767, claims 1-35 of U.S. Patent No. 6,743,779, claim 125 of U.S. Patent No. 5,830,430, claims 73-81 of U.S. Patent No. 6,056,938, and claim 12 of U.S. Patent No. 5,997,898. Although the conflicting claims are not identical, they are not patentably distinct from each other because the inventions claimed in the conflicting applications are species of, and therefore anticipate, the instant claim.

Claim 1 of the instant application is directed to a method for delivering a compound into a cell comprising administering a composition comprising the compound and an organic halide. The broadest claim of the '767 patent is directed to a method of expressing an exogenous nucleic acid in a cell (which would require introduction of the nucleic acid into the cell) comprising delivering the exogenous nucleic acid together with a halide compound into the cell and applying ultrasound sufficient to express the nucleic acid sequence in the cell. The method is fully embraced by a method comprising administering a composition comprising a compound and an organic halide and therefore anticipates the instant claim. Likewise, the broadest claim of the '779 application is limited to a method for delivering a nucleic acid into a cell comprising administering to the cell a composition comprising an RNA or DNA (*i.e.*, compound), a fluorinated organic compound (*i.e.*, organic halide) and a lipid carrier; claim 125 of the '430 patent is directed to a method of delivering intracellularly a bioactive agent (*i.e.*, compound) comprising contacting a cell with said bioactive agent, a cationic lipid of defined structure, and a specific fluorinated organic gas or gaseous precursor (*i.e.*, organic halide); and claim 73 of the '938 patent is directed to a method for delivering intracellularly a bioactive agent comprising contacting a cell with a cationic lipid of defined structure, a perfluorocarbon (*i.e.*, organic halide) and said bioactive agent. Each of these claims is fully encompassed by, and anticipates the instant claim 1.

Claim 12 of the '898 application is directed to a method for *in vivo* delivery of a bioactive agent comprising administering to a patient genetic material in combination with a stabilized vesicular composition of a fluorinated amphiphilic organic compound of defined structure and a gas, wherein said gas is sulfur hexafluoride and is encapsulated in vesicles which are selected

from the group consisting of liposomes, micelles and microspheres. Although the claim does not explicitly recited that the genetic material is delivered into a cell, the genetic material contemplated in the specification (column 26) would have to be delivered into a cell in order to provide the therapeutic outcome recited in the claim. Thus, absent evidence to the contrary, delivery into a cell is inherent to the method and the claim anticipates the instant claim 1.

As the limitations of each of the inventions claimed in the conflicting applications are fully encompassed by the instant claim 1, the instant claim is obvious over claims of U.S. Patent No. 6,638,767, U.S. Patent No. 6,743,779, U.S. Patent No. 5,830,430, U.S. Patent No. 6,056,938, and U.S. Patent No. 5,997,898.

Claim 1 is directed to an invention not patentably distinct from claim 125 of commonly assigned U.S. Patent No. 5,830,430, claims 73-81 of commonly assigned U.S. Patent No. 6,056,938, and claim 12 of commonly assigned U.S. Patent No. 5,997,898 (*Id.*), which name an inventive entity that is different from the inventive entity of the instant application.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). The commonly assigned applications discussed above would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting

inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for delivering a nucleic acid into a cell comprising administering a composition comprising a nucleic acid and an organic halide, wherein the composition further comprises a lipid carrier or wherein ultrasound is applied to said cell, does not reasonably provide enablement for the broad scope of a method of delivering any compound into a cell by administration of said compound with any organic halide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not

limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and Breadth of the claims: The claim broadly encompasses a method wherein a compound is introduced into a cell by administering said compound in a composition that further comprises an organic halide. Organic halide is defined in the fourth full paragraph on page 6 of the specification as a compound containing at least one carbon atom (or optionally sulfur or selenium atom) and at least one halogen atom selected from the group consisting of fluorine, chlorine, bromine or iodine. Thus, the organic halide of the claims broadly encompasses a very large genus of structurally and functionally divergent molecules. In the first full paragraph on page 15, the specification teaches, "[a] wide variety of compounds can comprise the compounds to be delivered to the cells in accordance with the invention, including bioactive agents, diagnostic agents, pharmaceutical agents, and the like, and include proteins, DNA and RNA..." Thus, the compound of the claims is of essentially unlimited scope. Furthermore, on page 14, the specification teaches, "[i]ntracellular delivery includes delivery into the cells through a cell membrane (plasma membrane), cell wall, and/or nuclear membrane" (second full paragraph).

Viewed as a whole, the claim encompasses a method of extraordinary breadth, wherein essentially any compound is delivered through a cell membrane, cell wall and/or nuclear membrane in combination with a compound containing at least one carbon atom (or optionally

sulfur or selenium atom) and at least one halogen atom selected from the group consisting of fluorine, chlorine, bromine or iodine. Although, the Office has acknowledged that the method is enabling for delivering a nucleic acid into a cell comprising administering a composition comprising a nucleic acid and an organic halide, wherein the composition further comprises a lipid carrier or wherein ultrasound is applied to said cell (U.S. Patent Nos. 6,638,767 and 6,743,779), the specification fails to enable the method beyond this scope.

State of the prior art and level of predictability in the art: First, with regard to delivery of a nucleic acid into a cell in the absence of a lipid carrier or the application of ultrasound, the art provides no specific guidance as to which organic halides would be operative in the method or what formulations of nucleic acid and organic halide would provide useful delivery of a nucleic acid into a cell. Godbey *et al.* (2001) *J. Control. Release* 72: 115-125 teaches that the ability of a given chemical compound to facilitate transport of a nucleic acid across the plasma membrane is unpredictable beyond the scope of liposomes and some cationic polymers. Godbey *et al.* teaches, "[o]ne point that has become clearer with each published report is that not all gene delivery vehicles operate in the same fashion. Even a simple modification of a delivery molecule can alter the cellular processing of the agent dramatically" (first full paragraph in the right column on page 119) and "[t]he reason behind the varying transfection efficiencies lies in the mechanism for each type of gene transfer, whether it is a difference in cellular entry routes or disparate DNA release kinetics" (paragraph bridging pages 119-120). Thus, Godbey *et al.* teaches that the critical parameters that enable even well characterized gene delivery vehicles such as lipids to transfer nucleic acids across the plasma membrane are not well understood and that even small changes in the structure of a molecule can have dramatic effects on its functional properties.

Given these teachings, the skilled artisan would not expect to be able to readily identify molecules within the scope of the organic halide of the claim capable of delivering a nucleic acid into a cell in the absence of a lipid carrier or the application of ultrasound.

With regard to the broader scope of delivering compounds other than nucleic acids into cells, the art teaches delivery of many compounds across cell walls and membranes has proved more difficult than for the structurally homogeneous nucleic acid molecule. For example, in spite of tremendous interest in delivering peptides and proteins into cells, there have been very molecules identified as capable of providing non-invasive delivery of peptides and proteins. Hawinger (1999) *Curr. Opin. Chem. Boil.* 3:89-94 teaches, "[t]he plasma membrane of eukaryotic cells is inherently impermeable to peptides and proteins that lack specialized membrane receptors or transport proteins" (paragraph bridging pages 89-90) and "invasive techniques of microinjection or applications of membrane-disrupting pore-forming reagents...are usually employed to introduce antibodies, synthetic peptides or other noncell membrane-permeable molecules into cells" (sentence bridging the left and right columns on page 89). Although Hawinger goes on to teach that a very limited number of peptide molecules have been identified as capable of facilitating intracellular delivery of some peptides and proteins (see especially Table 1), Veach *et al.* (2004) *J. Biol. Chem.* 279: 11425-11431 teaches that as of 2004 the mechanism by which these peptides translocate cargo across the plasma membrane remained unexplained (paragraph bridging the left and right columns on page 11425). Thus, the combined teachings of Hawinger and Veach *et al.* show that, even many years after the effective filing date of the instant application, development of methods to introduce a very large class of compounds (*i.e.*, peptides and proteins) into a cell was at a very early stage of development. Therefore, the

skilled artisan would not be able to readily practice the method as it encompasses delivery of peptides, proteins or other non-nucleic acid molecules into cells without specific guidance as to which organic halide compounds would be capable of providing transport across the membrane.

Amount of direction provided by the inventor and existence of working examples: The working examples disclosed in the instant application demonstrate enhanced delivery of nucleic acids into HeLa cells by treatment with ultrasound (Tables 5 and 6) into various cell lines by addition of perfluorohexane, bromononafluorobutane, perfluoropentane, perfluorooctane and perfluorodecane (Tables 7-13). However, the disclosure provides no working examples of the claimed method wherein a nucleic acid is delivered across the plasma membrane by an organic halide alone or delivery of any compound into a cell other than a nucleic acid.

Although the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation, In re Borkowski, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970), lack of a working example is a factor to be considered, especially in a case involving an unpredictable and undeveloped art. The art cited above clearly establishes that the ability to facilitate delivery of compounds such as nucleic acids and proteins across the plasma membrane of a cell is a characteristic of only a few compounds. Further, the art teaches that the structural characteristics that confer the ability to transport other molecules across the plasma membrane were not established such that, at the time of filing, the skilled artisan could readily identify an organic halide capable of delivering a compound across a plasma membrane. Thus, the relevant art is clearly established to be undeveloped and unpredictable. Although the specification suggests various preferred embodiments of the claimed invention (*e.g.*, Table 1), no evidence is

provided to indicate that any of these embodiments would have the capacity to deliver any compound across the plasma membrane of a cell in the absence of a lipid carrier or ultrasound and no evidence is provided to indicate that any compound other than a nucleic acid could be delivered into a cell according to the claimed method.

By way of theory, the specification provides, "it is believed that delivery of nucleic acid sequences and other compounds in accordance with the methods of the present invention may induce a cell to take up the compound to be delivered thereto. Included within the definition of delivery of a compound into a cell in accordance with the methods of the present invention are active and passive mechanisms of cellular uptake. Ion channels and other means of transport utilized by cells to incorporate extracellular materials, including compounds to be delivered thereto, into the intracellular milieu are encompassed by the present invention" (page 13). However, given the teachings from the art, which suggest that only a small fraction, if any, of the organic halides of the claims would be capable of facilitating transport of a compound across the plasma membrane in the absence of a lipid carrier or ultrasound, and the likelihood that no single organic halide would be capable of delivering a broad spectrum of structurally diverse compounds across the plasma membrane, one of ordinary skill in the art would not know which organic halide could be use to deliver any given compound into a cell.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, one of ordinary skill would not be able to practice the full scope of the claimed invention without engaging in undue experimentation. Given the expansive scope of the claimed subject matter, wherein essentially any organic halide is used to deliver essentially any compound into a cell, and the teachings from

the art which indicate that the ability of deliver a compound across the plasma membrane is an unpredictable property of a small set of compounds, the skilled artisan would expect that the claimed method encompasses a tremendous number of inoperative embodiments. Although the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled, *Atlas Powder Co. v. E.I. du Pont de Nemours & Co* (224 USPQ 409, 414; *Id.*) provides, "if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid" (page 414). The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984).

The skilled artisan seeking to practice the instant claimed method according to its full scope would be forced to identify which of the many thousands of combinations of organic halide and compound encompassed by the claim would be operative in a method of introducing a compound into a cell. By way of guidance in determining the operative embodiments of the invention, the specification provides only suggestions of preferred embodiments of the organic halide and very limited working examples, which provide the method practiced with a single compound (*i.e.*, DNA) and five species of organic halide, wherein the composition further comprises additional ingredients (*i.e.*, transfection reagents) that would provide delivery of a nucleic acid into a cell even in the absence of the organic halide. Given these teachings the skilled artisan would have no idea which embodiments of the claimed invention would be

operative, beyond those wherein the compound is a nucleic acid and the method further comprises a lipid carrier or application of ultrasound. Thus, operability of each of the many thousands of combinations encompassed by the claims would have to be determined independently by empirical experimentation. Clearly, therefore, determining which embodiments of the claimed invention that were conceived, but not yet made, would be inoperative or operative would require tremendous effort and places an undue burden on one of ordinary skill seeking to practice the invention. Therefore, the claim is rejected under 35 U.S.C. §112, first paragraph, as lacking enablement for the full scope of the claimed subject matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Unger (WO 94/28780).

Unger *et al.* teaches a method of expressing an exogenous nucleic acid sequence in a cell comprising the steps of: delivering said nucleic acid sequence to together with a halide compound into the cell. In the Examples beginning on page 70 and continued through page 87, Unger *et al.* teaches a method of making gaseous precursor-filled liposome microsphere or

microbubble and the administration of said microspheres with a variety of perfluorocarbons (see especially Table II). Unger *et al.* further teaches that these microspheres can be used to deliver genetic material-including RNA, DNA and antisense RNA-for expression in heterologous cells (see especially beginning the second full paragraph of page 64 and continued through the first paragraph on page 65), Thus, Unger *et al.* teaches a method comprising all of the elements of the instant claim 1; therefore, the claim is anticipated by Unger *et al.*

Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by either one of Kabanov *et al.* U.S. Patent No. 5,656,611 or Eppstein *et al.* U.S. Patent No. 5,550,289.

Kabanov *et al.* teaches a composition comprising a polynucleotide and an organic polymer with a lipid substituent and a fluoro or chloro substitution (column 8, line 45 through column 9, line 20) and methods of delivering the polynucleotide into a cell using the composition (see especially the first paragraph in column 1 and the Examples). As the organic polymer with a lipid substituent and a fluoro or chloro substitution anticipates the organic halide of the instant claim 1, the method contemplated by Kabanov *et al.* comprises all of the elements of the instant claim 1 and therefore anticipates the claim.

Likewise, Eppstein *et al.* teaches the introduction of DNA into a cell using a liposome (column 2, line 54), and a halide (column 8, line 7). The liposome of Eppstein *et al.* is made up of carbon atoms (column 3, line 20, Formula I) and preferably contains chlorine which is a halogen atom (see especially column 15, line 21). Thus, Eppstein *et al.* teaches a method of delivering a compound into a cell comprising all of the elements of the instant claim 1. Therefore, Eppstein *et al.* anticipates the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1 is rejected under 35 U.S.C. 103(a) as being obvious over any one of U.S. Patent No. 5,830,430, U.S. Patent No. 6,056,938, and U.S. Patent No. 5,997,898.

The applied reference has a common inventor and assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

As described above, each of the patents disclose subject matter that is fully encompassed by the instant claim 1 and therefore renders the generic claim obvious. To summarize, claim 125 of the '430 patent is directed to a method of delivering intracellularly a bioactive agent comprising contacting a cell with a cationic lipid of defined structure, and a specific fluorinated organic gas or gaseous precursor and claim 73 of the '938 patent is directed to a method for delivering intracellularly a bioactive agent comprising contacting a cell with a cationic lipid of

defined structure, a perfluorocarbon and said bioactive agent. Each of these claims is fully encompassed by, and renders obvious the instant claim 1.

Claim 12 of the '898 application is directed to a method for *in vivo* delivery of a bioactive agent comprising administering to a patient genetic material in combination with a stabilized vesicular composition of a fluorinated amphiphilic organic compound of defined structure and a gas, wherein said gas is sulfur hexafluoride and is encapsulated in vesicles which are selected from the group consisting of liposomes, micelles and microspheres. Although the claim does not explicitly recited that the genetic material is delivered into a cell, the genetic material contemplated in the specification (column 26) would have to be delivered into a cell in order to provide the therapeutic outcome recited in the claim. Thus, absent evidence to the contrary, delivery into a cell is inherent to the method and the claim renders obvious the instant claim 1.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M Sullivan, Ph.D.
Examiner
Art Unit 1636